Prevention of non-ventilator-associated hospital-acquired pneumonia in Switzerland: a type 2 hybrid effectiveness–implementation trial

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Summary

Background Non-ventilator-associated hospital-acquired pneumonia (nvHAP) is a frequent, but under-researched infection. We aimed to simultaneously test an nvHAP prevention intervention and a multifaceted implementation strategy.

Methods In this single-centre, type 2 hybrid effectiveness–implementation study, all patients of nine surgical and medical departments at the University Hospital Zurich, Switzerland, were included and surveyed over three study periods: baseline (14–33 months, depending on department), implementation (2 months), and intervention (3–22 months, depending on department). The five-measure nvHAP prevention bundle consisted of oral care, dysphagia screening and management, mobilisation, discontinuation of non-indicated proton-pump inhibitors, and respiratory therapy. The implementation strategy comprised department-level implementation teams who conducted and locally adapted the core strategies of education, training, and changing infrastructure. Intervention effectiveness on the primary outcome measure of nvHAP incidence rate was quantified using a generalised estimating equation method in a Poisson regression model, with hospital departments as clusters. Implementation success scores and determinants were derived longitudinally through semistructured interviews with health-care workers. This trial is registered with ClinicalTrials.gov (NCT03361085).

Findings Between Jan 1, 2017, and Feb 29, 2020, 451 nvHAP cases occurred during 361 947 patient-days. nvHAP incidence rate was 1·42 (95% CI 1·27–1·58) per 1000 patient-days in the baseline period and 0·90 (95% CI 0·73–1·10) cases per 1000 patient-days in the intervention period. The intervention-to-baseline nvHAP incidence rate ratio, adjusted for department and seasonality, was 0·69 (95% CI 0·52–0·91; p=0·0084). Implementation success scores correlated with lower nvHAP rate ratios (Pearson correlation –0·71, p=0·034). Determinants of implementation success were positive core business alignment, high perceived nvHAP risk, architectural characteristics promoting physical proximity of health-care staff, and favourable key individual traits.

Interpretation The prevention bundle led to a reduction of nvHAP. Knowledge of the determinants of implementation success might help in upscaling nvHAP prevention.

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Introduction

Hospital-acquired pneumonia contributes the highest number of disability-adjusted life-years among the six major health-care-associated infections,[1] with non-ventilator-associated hospital-acquired pneumonia (nvHAP) representing 60–70% of cases.[2,3] As a consequence, around half of patients with nvHAP require intensive care unit admission,[4] many have a long hospital stay,[4] 20% need mechanical ventilation,[4] and up to 30% have a fatal in-hospital outcome.[5] However, previous research has focused almost exclusively on ventilator-associated pneumonia. In recent years, prevention initiatives have started to consider nvHAP.[6] Notably, in 2022, the Society of Healthcare Epidemiology of America guideline for the first time included a section on nvHAP prevention, although little robust data existed on intervention strategies.[7]

Traditionally, effectiveness studies have been used to evaluate interventions and implementation studies to test strategies for delivering the intervention. Combining both study types in a hybrid approach produces simultaneous results on the effectiveness of the intervention and its implementation.[8] This approach helps to provide understanding and to facilitate replication and scale-up of a new intervention more broadly and rapidly. We aimed to conduct a type 2 hybrid effectiveness–implementation study to evaluate the effect of a prevention intervention and multifaceted implementation strategy on nvHAP incidence rates and implementation outcomes.

Methods

Study design and participants

This type 2 hybrid effectiveness–implementation trial with a quasi-experimental, non-randomised,

Research in context

Evidence before this study

Although non-ventilator-associated hospital-acquired pneumonia (nvHAP) is one of the most common health-care-associated infections, guidelines and the scientific literature on the prevention of nosocomial pneumonia focus primarily on ventilator-associated pneumonia. Additionally, although evidence exists for the effectiveness of single preventive measures, such as oral care, little is known about the effectiveness of prevention bundles. We searched PubMed for studies published in English, German, or French between Jan 1, 2000, and Aug 1, 2022, using the search terms ("prevention" OR "prophylaxis") AND "pneumonia" AND ("postoperative" OR "hospital-acquired" OR "healthcare-associated") AND ("randomised controlled trial" [publication type]) OR ("cohort studies" OR "case-control studies" OR "quality improvement" OR "controlled before-after studies" OR "interrupted time series analysis" OR "retrospective studies" [MESH terms]) NOT ("ventilator" OR "COVID"). We also searched reference lists of relevant articles for additional sources. Several previous studies found prevention bundles to be effective against postoperative pneumonia in surgical patients, but few strictly differentiated between ventilator-associated pneumonia and nvHAP. Since 2020, three studies reported an nvHAP prevention bundle that included non-surgical patients. First, a small (n=123) randomised controlled trial in a geriatric ward did not show any effect of a multicomponent intervention on nvHAP rates. Second, an nvHAP prevention bundle showed a reduction in pneumonia among a patient population on tube feeding. Third, a large cohort study in a broad patient population showed a successful reduction of nvHAP rates but, unfortunately, lacked a standard nvHAP definition. All prevention bundles for postoperative pneumonia and nvHAP included an oral care component, in addition to other elements such as mobilisation, respiratory therapy, and elevation of head of bed. None of the identified studies investigated the implementation process itself.

Added value of this study

The current study is unique in investigating the effectiveness of an intervention to introduce a five-measure nvHAP prevention bundle using a multifaceted implementation strategy in a broad surgical and medical patient population, while applying an established nvHAP definition (European Centre for Disease Prevention and Control). This hybrid type 2 trial simultaneously evaluated implementation and effectiveness outcomes. The results showed not only that the prevention intervention effectively lowered the nvHAP incidence rate by 31% (adjusted rate ratio 0·69 [95% CI 0·52–0·91]) but also revealed how key determinants influenced the implementation of the nvHAP bundle. All-cause in-hospital mortality in the entire study population did not change significantly (0·92 [0·81–1·04]).

Implications of all the available evidence

nvHAP is a frequent health-care-associated infection affecting a broad patient population. A combination of prevention measures including oral care, screening and managing of dysphagia, discontinuation of non-indicated proton-pump inhibitors, mobilisation, and respiratory therapy effectively reduced nvHAP incidence rate. Implementation success was associated with the preventive effect. The implementation strategy was described, as well as contextual individual and organisational factors associated with implementation success. Knowledge of these factors could help to promote nvHAP prevention in other health-care settings. Importantly, the distinctive description of implementation and intervention effectiveness can be especially helpful in the future upscaling of nvHAP prevention initiatives.

stepped-wedge design (figure 1) was conducted at the University Hospital Zurich (Zurich, Switzerland), a 950-bed tertiary-care teaching hospital that includes all medical specialities except paediatrics and orthopaedics. The hospital has a dedicated infection-prevention team and a goal-oriented infection-prevention campaign under hospital leadership that includes the surveillance of other frequent health-care-associated infections, monitoring of corresponding prevention measures, and feedback of results to departments.

We included all patients admitted to six medical and three surgical departments with an nvHAP rate above the 50th percentile among all departments in 2017. Three study periods were defined: the baseline period, starting in January, 2017, for all departments; a 2-month implementation period, during which initial implementation activities commenced, starting (at the discretion of each department) between March, 2018, and October, 2019; and the intervention period, originally planned until October, 2020, but terminated prematurely on Feb 29, 2020, because of the COVID-19 pandemic (figure 2).

A formal ethics evaluation was waived by the ethics committee of the Canton of Zurich, Switzerland (Req-2017-00731). The study is reported according to the Standards for Reporting Implementation Studies checklist.[9]

The study protocol was registered with ClinicalTrials.gov (NCT03361085) and has been published.[10]

Intervention

The nvHAP bundle consisted of five prevention measures: oral care, dysphagia screening and management, mobilisation, discontinuation of non-indicated proton-pump inhibitors, and respiratory therapy (panel). We selected intervention measures on the basis of existing literature and of their anticipated feasibility and ease of implementation.

The multifaceted implementation strategy was based on existing frameworks and designed to allow for local adaptation and ownership.[12–14] Department

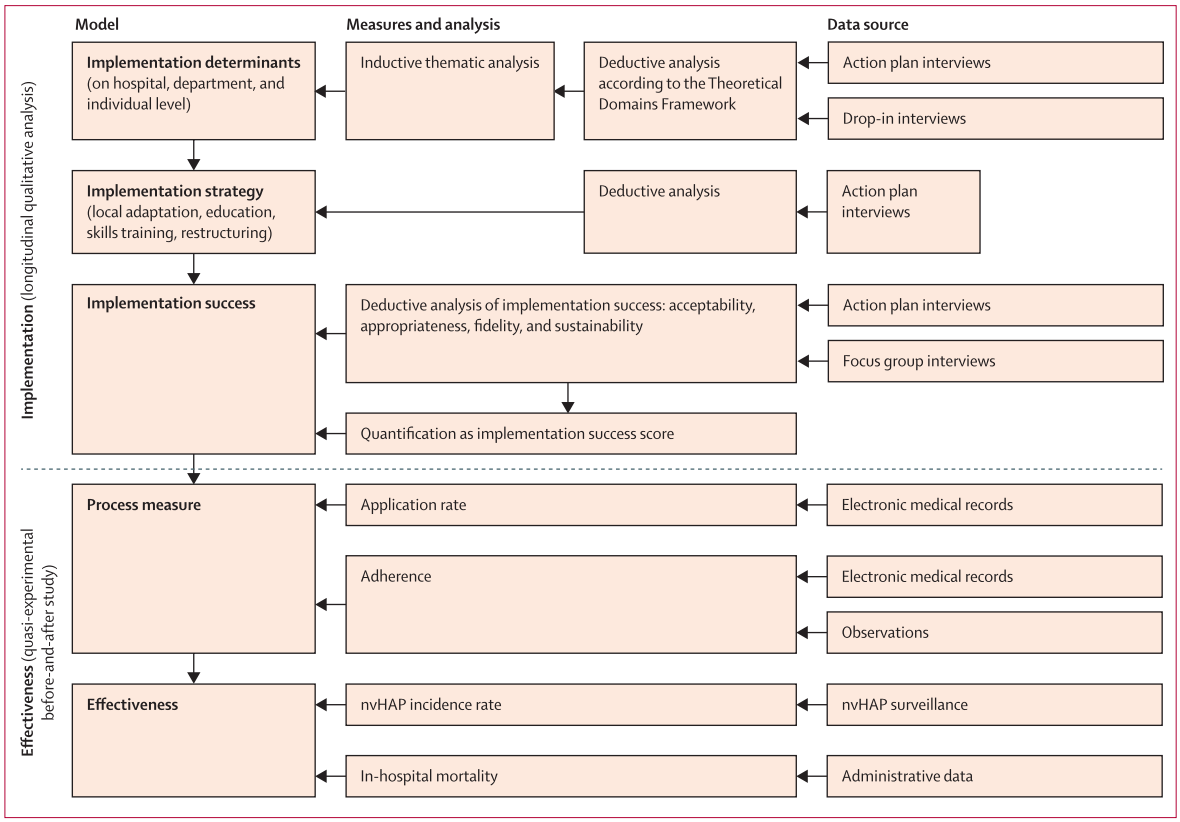

Figure 1: **Type 2 hybrid effectiveness–implementation study model and measures**
The conceptual model posits that the implementation determinants, also representing the context (ie, the characteristics of the organisation, departments, and involved individuals), influence the selection and performance of implementation strategies of the departments (not part of this report), resulting in varying levels of implementation success reflected by nvHAP bundle adherence, the application rate of prevention measures and, ultimately, the nvHAP incidence rate. The diagram also includes the means of evaluating the implementation and effectiveness at the different levels of the model and the corresponding data. nvHAP=non-ventilator-associated hospital-acquired pneumonia.

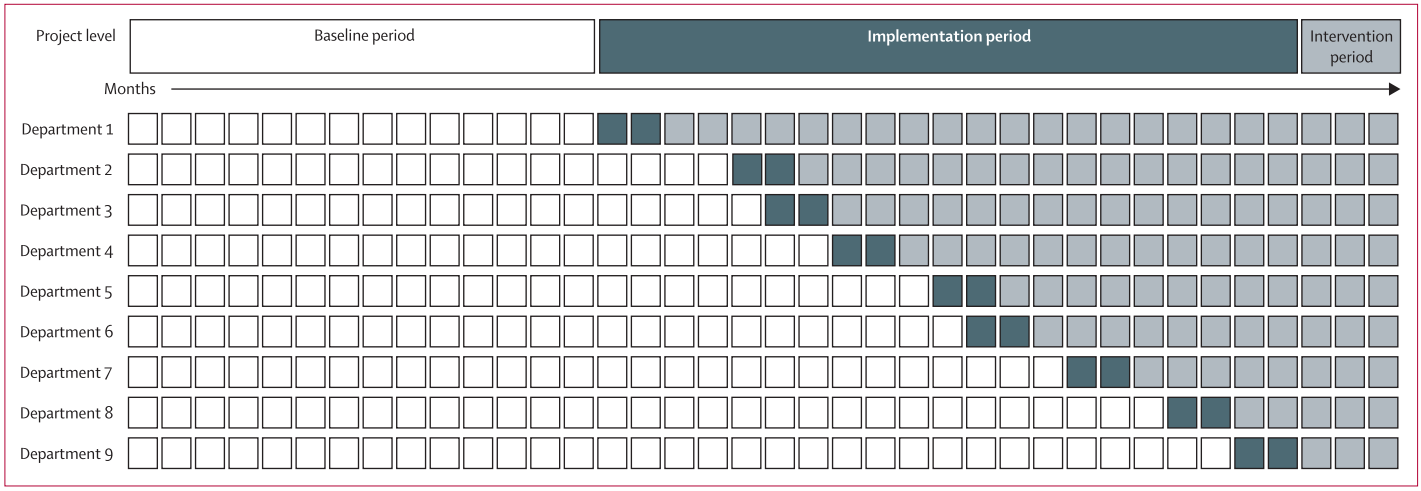

Figure 2: **Timeline of study periods**
Study periods at the department and project levels. Each square represents 1 month for each department.

implementation teams included a nurse, a physician, and a physiotherapist. These delegates were responsible for sustaining the core implementation strategies of education, skill training, infrastructure adaptation (ie, modifying the physical structure, equipment, record systems, and policies to support the delivery of the intervention), and adapting strategies to local needs (appendix pp 2–4).[10] An institutional implementation

See Online for appendix

Panel: **Intervention bundle elements**

Oral care

Patients required mechanical oral care (eg, tooth brushing) at least once per day, either executed by the patients themselves, if a good quality of oral care could be guaranteed, or otherwise executed or assisted by a nurse. Patients with dysphagia required mechanical oral care three times per day. Pharmacological oral care with chlorhexidine (mostly twice per day) was required for patients with relevant pathologies of the mouth (eg, severe gingivitis or periodontitis), as prescribed by the physician. Referral to dental treatment was required if indicated and prescribed by the physician.

Dysphagia screening and management

A modified swallowing assessment (MSA) adapted from the Standardized Swallowing Assessment by Perry[11] was used to screen for dysphagia at the bedside (appendix p 32). Screening with the MSA was done for each patient meeting at least one of the following criteria: neurological or neuromuscular disease; major thoracic, abdominal, or facial-oral surgery; and need for assisted oral care. If MSA screening indicated risk of aspiration, the patient was referred to a facial-oral tract therapist or a speech therapist for further evaluation and treatment. Until further evaluation, the patient should ideally have no oral intake or, as a minimum requirement, a structure-modified diet. Further evaluation of dysphagia resided with the responsible physicians, nurses, and therapists, including video fluoroscopy or functional endoscopic evaluation, and could lead to treatment including swallowing exercises, oral stimulation, structure-modified diet, or enteral and parenteral nutrition.

Mobilisation

Every patient without contraindication required mobilisation at the bedside (sitting on the edge of the bed) or out of the bed at least twice per day. Early postoperative mobilisation (ie, mobilisation out of bed or at the bedside on the day of surgery) was mandatory after surgery. Mobilisation could either be executed by the patient or assisted by nurses or physiotherapists.

Discontinuation of non-indicated proton-pump inhibitors

Proton-pump inhibitors were restricted to an in-house indication list.

Respiratory therapy

Responsible physicians were advised to refer the following patients to respiratory therapy: patients with chronic pulmonary disease; patients who required more than 3 L of oxygen to reach an oxygen saturation of more than 93%; patients recovering from abdominal or thoracic surgery or injury; patients who were not out of bed for more than 4 h/day; and patients having problems with coughing and at risk for accumulating bronchial secretions. Respiratory therapy was at the discretion of the physiotherapist and could include manual or assisted respiratory therapy and mucolysis, therapeutic body positioning, and activation and mobilisation.

team (AW, LC, and MFH) supported department implementation teams to establish and continuously adapt their action plans and implementation goals and provided them with educational and training materials. A formative approach was applied, with interim qualitative and quantitative results constantly used to enhance local implementation.[15]

Data collection and outcomes

The study assessed five outcome measures: nvHAP incidence rate, all-cause in-hospital mortality, process measures, implementation determinants, and implementation success (figure 1).[10]

The primary outcome was the nvHAP incidence rate per 1000 patient-days, aggregated by department and month. nvHAP cases were recorded retrospectively by a validated semiautomated surveillance system by applying European Centre for Disease Prevention and Control definitions (appendix p 5).[16,17] In brief, the pneumonia definition comprises radiological criteria, systemic signs (fever >38°C, leukopenia, or leukocytosis), and pulmonary symptoms (eg, cough or sputum production), while microbiological criteria are optional.

The secondary outcome, all-cause in-hospital mortality, was assessed on the basis of administrative data. Length of hospital stay was listed as a secondary outcome in the study protocol but was not analysed because of unavailability of the required data. The covariate case mix index (CMI), defined as mean case severity (ie, the sum of the cost weights, according to Swiss diagnosis-related groups,[18] divided by the number of cases) within a specific department and month, was extracted from administrative data.

Process measures were assessed in two ways: application rate per 1000 patient-days, established from electronic medical record data and aggregated by department and month (appendix p 6); and adherence proportion, assessed through manual data extraction and patient interrogation in a convenience sample of 50 patients per department at baseline and three times during the intervention (appendix p 7).[10]

Implementation success was described qualitatively in terms of four implementation outcomes (acceptability, appropriateness, fidelity, and sustainability; appendix p 8),[19] and quantified (as an exploratory outcome) as implementation success scores. Implementation determinants were established from qualitative data. Data for the implementation success and implementation determinants outcome measures were collected longitudinally through action plan interviews with department implementation teams once during the baseline period and twice during the intervention period, as well as through drop-in interviews with front-line staff once during the baseline period and three times during the intervention period, and through focus groups with interprofessional front-line staff once at the end of the intervention period (appendix p 9). Qualitative data collection was guided by the concept of high information power.[20]

Statistical analysis

Sample size estimation was based on the binomial approximation of rates. In 2017, the incidence of nvHAP in the departments included in our study was 153 events among a total of 13 591 patients. We expected a reduction of this incidence due to our prevention bundle by 30% during the intervention phase. To show the difference between these two rates with a power of 80% at a significance level of 5%, we estimated that a total of 250 events would be required. The calculation

was done with Stata software (release 15). We concluded that a 1-year baseline (with 153 events) and a 1-year intervention period (with 107 expected events) would be sufficient.

The number of nvHAP cases and patient-days per study period and department were descriptively reported with unadjusted nvHAP rate ratios (RRs) between the intervention and baseline periods. An adjusted nvHAP RR to quantify the effectiveness of the intervention in reducing the nvHAP rate was estimated by a Poisson generalised estimating equation (GEE) with log link, with departments as clusters. The GEE was fitted to the monthly numbers of nvHAP cases per department with the number of patient-days (in thousands) as offset. A first-order, autoregressive correlation structure was used to account for the temporal correlation of nvHAP rates within departments. A time-dependent, department-specific binary indicator for the intervention was used as an explanatory variable, with baseline coded as 0, implementation as 0·5, and intervention as 1. Department was added to adjust for differences in baseline nvHAP rates among departments and sine–cosine waves (frequency $\omega = 2\pi / 12$) were added to adjust for seasonality over the monthly measurements. All-cause in-hospital mortality was analysed accordingly. Because of the early termination of the study after only 3 months of intervention at the project level, the planned analysis comparing study periods at the project level was not included in the main results, but is reported in the appendix (p 10).

Three sensitivity analyses were done for nvHAP and mortality. First, to assess a potential regression-to-the-mean effect, the GEE was refitted with exclusion of data from 2017 (because we included departments in our study with relatively high nvHAP incidence rates in 2017 and thus a potential reduction might be due to regression to the mean). Second, to assess whether a change in the CMI of the patients might have confounded the nvHAP bundle effect, we added the CMI (available per department and month) as an explanatory variable to the GEE. Third, to assess confounding by another (unexpected) trend over time, the study month was added as an explanatory variable to the GEE. To further estimate the effectiveness of the intervention within individual departments, a Poisson generalised linear mixed-effects model (GLMM) with a random intercept and a random intervention effect per department was fitted to the department-level data and adjusted for seasonality. We then calculated the Pearson correlation coefficient between department-specific RR estimates for the intervention effect and the implementation success score in the corresponding department.

Prevention measure application rates were compared between study periods using negative binomial GLMMs (overdispersion regarding Poisson) on counts of each measure, with patient-days in thousands as offset. Because there were many zero counts from bedside dysphagia screening, especially during the baseline period, this process measure was modelled with a zero-inflated Poisson GLMM. Binominal GEEs were used to compare the proportion of patients with adherence to prevention measures between the four visits (at baseline and at months 1–2, 3–5, and 8–10 of the intervention period).

To further assess whether the implementation success score was associated with nvHAP rates and whether the intervention effect changed depending on it, we included the implementation success score and the interaction of this score with the intervention as additional terms in the primary GEE model.

Data were analysed with use of R (version 4.2.1).

Qualitative analysis

Implementation success was primarily evaluated by coding the longitudinal qualitative data according to the four implementation outcomes: acceptability, appropriateness, fidelity, and sustainability.[19] By assessing implementation outcomes at three timepoints, we aimed to identify leading and lagging indicators of implementation success;[19] leading indicators are those that reflect the outcome of a change in practice early on or even predict it, and lagging indicators reflect the delay between a change in practice and the observable outcomes. To quantify implementation success for inclusion in the department-level GEE model, three researchers (MFH, LC, and AW) reviewed excerpts from interview transcripts coded according to implementation outcomes. They rated the degree of the four outcomes per department, professional group, and study period on a scale from 1 (very poor) to 7 (exceptional). Discrepancies among reviewers were discussed to reach consensus. Ratings of the four outcomes and three professions (physicians, nurses, and physiotherapists) were averaged, resulting in one implementation success score per department and study period. Implementation success scores from the last assessment were used for comparison with the intervention effect.

To analyse the effect of implementation determinants on implementation success, all interview transcripts and notes were first coded deductively with use of the Theoretical Domains Framework as a coding scheme (appendix p 11–12).[14] Second, inductive thematic analyses were conducted to identify themes relevant to implementation within these domains. Analyses began at the department level to assess implementation success considering local barriers and facilitators. Cross-case matrices were then used to explore trends across departments.

Role of the funding source

The funder of the study was not involved in study design, data collection, data analysis, data interpretation, or writing of the report.

	Total across study periods			Baseline period			Implementation period			Intervention period			Unadjusted RR (95% CI)	p values
	nvHAP count	Patient-days, thousands	nvHAP incidence rate (per 1000 patient-days)	nvHAP count	Patient-days, thousands	nvHAP incidence rate (per 1000 patient-days)	nvHAP count	Patient-days, thousands	nvHAP incidence rate (per 1000 patient-days)	nvHAP count	Patient-days, thousands	nvHAP incidence rate (per 1000 patient-days)		
Department 1	11	14·52	0·76	7	4·74	1·48	0	0·66	0·00	4	9·13	0·44	0·30 (0·09–1·01)	0·052
Department 2	72	57·17	1·26	38	30·57	1·24	7	3·29	2·13	27	23·31	1·16	0·93 (0·57–1·53)	0·78
Department 3	28	37·93	0·74	16	18·72	0·85	2	1·51	1·32	10	17·69	0·57	0·66 (0·30–1·46)	0·31
Department 4	41	49·60	0·83	27	27·08	1·00	2	2·62	0·76	12	19·90	0·60	0·60 (0·31–1·19)	0·15
Department 5	58	38·97	1·49	52	26·85	1·94	0	1·58	0·00	6	10·53	0·57	0·29 (0·13–0·68)	0·0045
Department 6	16	14·67	1·09	9	9·63	0·93	0	0·77	0·00	7	4·27	1·64	1·75 (0·65–4·71)	0·27
Department 7	73	54·75	1·33	60	41·42	1·45	2	2·79	0·72	11	10·54	1·04	0·72 (0·38–1·37)	0·32
Department 8	59	29·84	1·98	48	23·49	2·04	4	2·17	1·84	7	4·18	1·68	0·82 (0·37–1·81)	0·62
Department 9	93	64·49	1·44	81	55·82	1·45	2	3·72	0·54	10	4·95	2·02	1·39 (0·72–2·68)	0·32
All departments	451	361·95	1·25	338	238·33	1·42	19	19·12	0·99	94	104·50	0·90	0·63 (0·50–0·80)	<0·0001

Unadjusted RR estimates were calculated as the intervention period nvHAP rate divided by the baseline period nvHAP rate. Note that the overall estimate (all departments) reported in the Results (RR 0·69 [95% CI 0·52–0·91]) is adjusted for department and seasonality, and therefore slightly differs from the unadjusted estimate shown in the final row of this table. Likewise, the department-specific RRs estimated by the generalised linear mixed-effects model (range 0·49–0·77, as reported in the Results; appendix p 30) are adjusted for seasonality and vary less than the unadjusted estimates shown in this table because of partial pooling. nvHAP=non-ventilator-associated hospital-acquired pneumonia. RR=rate ratio.

Table: **nvHAP cases, patient-days, and nvHAP incidence rate per department and study period**

Results

Between Jan 1, 2017, and Feb 29, 2020, 451 cases of nvHAP occurred across 361 947 patient-days: 338 cases and 238 328 patient-days in the baseline period (incidence rate 1·42 cases [95% CI 1·27–1·58] per 1000 patient-days), 19 cases and 19 120 patient-days in the implementation period (0·99 [0·63–1·56]), and 94 cases and 104 498 patient-days in the intervention period (0·90 [0·73–1·10]).

The department-adjusted and seasonality-adjusted RR between the intervention and baseline periods was 0·69 (95% CI 0·52–0·91; p=0·0084), corresponding to a 31% reduction in the nvHAP incidence rate. Results per department and study period are shown in the table. Project-level results showed a trend in the same direction without reaching statistical significance (nvHAP RR for 3-month intervention *vs* 14-month baseline period 0·72 [95% CI 0·47–1·07], p=0·12; appendix p 10). A seasonal effect with a peak in winter was detected (appendix p 13). All sensitivity analyses showed a similar or even slightly stronger effect of the nvHAP bundle: RR 0·68 (0·51–0·92; p=0·0110) when excluding the year 2017, 0·66 (0·52–0·85; p=0·0012) when including CMI as an explanatory variable; and 0·63 (0·49–0·81; p=0·0004) when including the study month as an additional explanatory variable.

Overall, 1558 patients died from any cause during their hospital stay: 1024 in the baseline period, 83 in the implementation period, and 451 in the intervention period. On the basis of these numbers, the average mortality rate per 1000 patient-days was 4·30 (95% CI 4·04–4·57) during the baseline period, 4·34 (3·50–5·38) during the implementation period, and 4·32 (3·94–4·73) during the intervention period. The adjusted RR for in-hospital mortality was 0·92 (95% CI 0·81–1·04; p=0·18). Results were similar in the sensitivity analyses: RR 0·88 (95% CI 0·72–1·06; p=0·17) when excluding the year 2017, 0·90 (0·82–0·99; p=0·038) when including CMI as an additional explanatory variable, and 0·91 (0·68–1·21; p=0·50) with the study month as an additional explanatory variable.

Figure 3A shows the prevention measure application rate during the three study periods. Bedside dysphagia screening increased (RR 3·44 [95% CI 2·10–5·64], p<0·0001) and prescription of proton-pump inhibitors decreased (0·90 [0·86–0·93], p<0·0001) in the intervention period compared with the baseline period. Changes in oral care (1·09 [0·97–1·23], p=0·14), mobilisation (0·96 [0·90–1·03], p=0·26), and physiotherapy (0·99 [0·94–1·04], p=0·72) were non-significant. In line with the corresponding application rates, compared with baseline, improvements were observed in the proportions of patients with adherence to dysphagia screening and management (odds ratio 1·72 [95% CI 0·97–3·04] p=0·064) and discontinuation of non-indicated proton-pump inhibitors (2·01 [1·30–3·10], p=0·002) at the visit after 8–10 months of intervention,

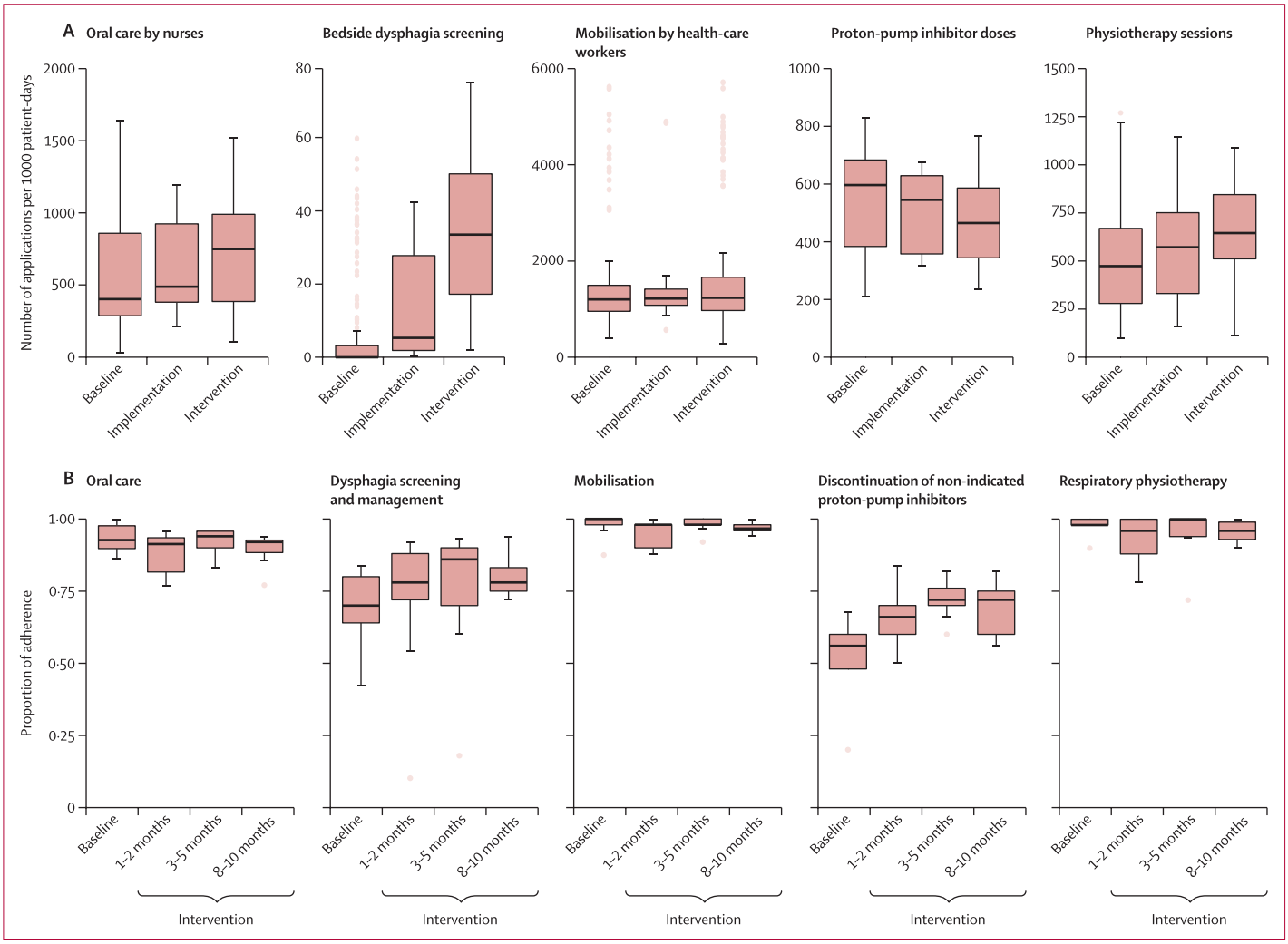

Figure 3: **Process measures**
(A) Application rates of nvHAP bundle prevention measures per 1000 patient-days in each department-level period. The boxplots summarise all monthly measurements per period (213 at baseline, 18 at implementation, and 111 at intervention). (B) Adherence to nvHAP bundle prevention measures. Boxplots show the proportion of patients in the sample with adherence to prevention measures by visit (baseline or after 1–2, 3–5, or 8–10 months of intervention). There are nine measurements per visit (one for each department), except for the visit after 8–10 months, when only seven measurements were available. All boxplots show the median (thick horizontal line), first and third quartiles (lower and upper ends of the box), and range (whiskers) excluding outliers (shown as individual datapoints and defined as values further than 1·5 × IQR above the third quartile or below the first quartile). nvHAP=non-ventilator-associated hospital-acquired pneumonia.

whereas oral care (0·60 [0·26–1·38], p=0·23), mobilisation (0·76 [0·20–2·87], p=0·68), and respiratory therapy (0·55 [0·22–1·41], p=0·22) did not change significantly in this period (figure 3B). Results per department are shown in the appendix (pp 14–23).

Longitudinal qualitative data were collected during 27 action plan interviews, 160 drop-in interviews, and nine focus group interviews. These data informed formative adaptation of the implementation process, identification of relevant implementation determinants, and evaluation of implementation success. For example, early interviews revealed that two relevant stakeholder groups—patients and patient hospitality services—should be actively involved in nvHAP prevention. Patients who were perceived by staff as independent were initially left out of oral care and mobilisation efforts. Implementation efforts were accordingly adapted to include patient-targeted communication (eg, stickers on patient mirrors to encourage self-initiated tooth brushing). Patient hospitality services became instrumental in motivating patients to eat in a seated position to decrease the risk of aspiration. Targeted education sessions on nvHAP risk factors consequently included hospitality services as partners in nvHAP prevention.

Overall, implementation success varied across departments and could be qualitatively explained by four inductively identified implementation determinants: core business alignment, perceived nvHAP risk, physical proximity, and key individual traits. These results are

detailed below and illustrated with quotes and in graphs in the appendix (pp 24–27, 28–29).

Acceptability of various elements of the intervention was high across departments and study periods among physiotherapists, who described the nvHAP measures as being aligned with their core business. Factors leading to low acceptability among all professional groups included perceived suboptimal timing of the project and the introduction of nvHAP measures alongside too many other activities as part of the hospital-wide infection-prevention initiative. Factors leading to high acceptability included perception that nvHAP measures led to observable improvements and high-quality patient care; attractive implementation materials and meaningful events; and, in some cases, perception that the project required little additional effort. Acceptability outcomes were also closely related to the theme of key individual traits (ie, the characteristics of people in participating departments, including, but not limited to, local delegates). Specifically, positive attitudes and charisma, intrinsic motivation, and the authority and latitude to make decisions while remaining in touch with the front-line were important facilitators. In most departments, acceptability among nurses (and to a lesser extent among physicians) increased throughout the project.

Similar to acceptability, appropriateness (ie, the perceived context fit of the intervention) varied among nurses and physicians across departments, while remaining high among physiotherapists. The perception of appropriateness was largely driven by perceived nvHAP risk (ie, the extent to which participants perceived their patients to be at risk of developing or having a high burden of nvHAP), and core business alignment (ie, how well the intervention aligned with existing departmental and professional activities and was perceived as being an integral part of their medical specialty). In departments where appropriateness was initially perceived to be low, audits and feedback of nvHAP rates and process indicators by the nvHAP project team were often successful in improving motivation and changing valency among local nvHAP teams.

Appropriateness and acceptability were leading indicators of implementation fidelity, which was also high among physiotherapists. Factors leading to high fidelity included key individuals who had the above-mentioned traits and positive attitudes in combination with organisational leverage to execute changes. These individuals helped to overcome challenges, such as high turnover or limited time resources, which would have otherwise hindered nvHAP implementation. By contrast, fidelity was particularly low if the departmental implementation team(s) felt little responsibility for the project or if turnover affected local delegates themselves, which occurred rarely. The physical proximity of health-care professionals made possible by certain architectural features (eg, multiple wards from a single department being situated close to each other with nursing and physician offices located nearby) facilitated interprofessional cooperation and led to higher implementation fidelity and adaptation of implementation strategies to local needs. In general, fidelity was lowest among physicians, mainly due to perceived lack of time resources or low prioritisation. Perceived lack of time was also pronounced among nurses for the mobilisation measure.

Sustainability (ie, the extent of integration of nvHAP measures into routines, making them likely to extend beyond the project duration) was assessed in the implementation and intervention periods. Higher sustainability was observed in professional groups and departments with higher acceptability and appropriateness. Sustainability was substantial among nurses of some (mostly medical) departments whose core business aligned with the nvHAP bundle measures. Sustainability was also high among physiotherapists, who were already professionally attuned to the importance of nvHAP prevention measures. Most physicians did not integrate processes supporting the intervention into their established operations. However, key individual traits were here counteractive: some motivated and skilled physicians established sustained changes in electronic health record systems and institutionalised training, even despite low core business alignment.

Implementation success scores (on a scale from 1 [very poor] to 7 [exceptional]) at the end of the intervention ranged from 3·9 to 6·5 (appendix p 30). Seasonality-adjusted, department-specific nvHAP incidence RRs estimated by GLMMs were between 0·77 and 0·49, corresponding to reductions of 23–51%. A higher implementation success score correlated with a lower nvHAP incidence RR (Pearson correlation –0·71, p=0·034; appendix p 30), and an increase of 1·0 in implementation success score was associated with a reduction in nvHAP RR by a factor of 0·66 (95% CI 0·47–0·92; appendix p 31).

Discussion

This type 2 hybrid study investigated the effectiveness and implementation of an intervention to reduce nvHAP through a five-measure prevention bundle and a multifaceted implementation strategy in nine medical or surgical departments in a tertiary-care centre. The intervention led to a significant and clinically relevant reduction of the nvHAP rate by 31%, but no statistically significant reduction in all-cause in-hospital mortality in the main model. Department-specific reductions in nvHAP rates correlated with implementation success. Qualitative analysis found that departments' positive core business alignment, high perceived nvHAP risk, favourable key individual traits in local delegates, and architectural characteristics promoting interprofessional physical proximity were drivers of this success. These findings are important because they underpin

the preventability of nvHAP while elucidating the implementation mechanisms of a successful multifaceted intervention.

Pre-existing literature on the effect of prevention bundles on nvHAP, as well as on implementation strategies, is scarce. A multicentre study found a significant reduction in unadjusted nvHAP incidence, from 5·92 to 1·79 per 1000 admissions, after implementing a bundle including mobilisation, upright feeding, swallowing evaluation, sedation restrictions, elevation of head of bed, oral care, and tube care.[21] Unfortunately, the study lacked a standard definition of nvHAP. Another study that included patients on enteral feeding showed a 34% reduction in nvHAP incidence when implementing a bundle including oral and nasal care, elevation of head of bed, and daily review of tube fixation.[22] Other authors investigated prevention bundles focusing on postoperative pneumonia, which often included chemical or mechanical oral care, mobilisation, elevation of head of bed, and respiratory therapy, and reported reducing nvHAP incidence by 40–80%.[23,24] These findings and our results show that the preventable proportion of nvHAP cases is similar to that of other health-care-associated infections.[25] However, our study is unique in employing a well established nvHAP definition, including medical and surgical departments, adjusting for seasonality, accounting for departments as clusters in the analysis, and evaluating implementation success and determinants together with effectiveness in a mixed-methods, quasi-experimental, type 2 hybrid approach. The uniqueness of our approach extends to a theoretically grounded implementation strategy based on department-level ownership, education, training, and changing infrastructure, with ongoing local adaptation through the feedback of qualitative findings by the institutional implementation team. Distinguishing implementation from intervention effectiveness is crucial for the successful upscaling of an intervention.[19]

With awareness of the inherent challenges in measuring care-protocol adherence, we assessed process measures in two ways. The prevention measure application rate included all patients continuously but did not consider the requirement for each prevention measure per patient and day. Prevention measure adherence did not have this shortcoming, but was restricted to a convenience sample of 50 patients per department at four study points. Two prevention measures (dysphagia screening and management and discontinuation of non-indicated proton-pump inhibitors) showed improvement in both assessment methods. The remaining three bundle elements showed non-significant changes in both metrics. Dysphagia screening was newly introduced in seven departments, which resulted in a steep increase in its use. Drop-in interviews confirmed the increased awareness among caregivers regarding the pathophysiological importance of aspiration and also of the preventive effect of oral care. Improvement in quality rather than quantity and missing documentation of single oral care events, which were mentioned in several interviews (appendix pp 24–27), might explain the absence of significant change in oral care process indicators. Mobilisation showed an adherence of more than 95% at baseline, preventing substantial improvement and indicating that the goal for mobilisation could be set higher.

To maximise its practical value, this study was designed as a type 2 hybrid trial, testing the implementation process simultaneously with its effect. In the qualitative analysis, we found high acceptability and appropriateness of the intervention to be leading factors for fidelity and sustainability in later study periods, which could be further explained by the implementation determinants. Although the importance of key individuals and their ability to counterbalance challenges is well known, the theme of core business alignment might be novel. Increasing specialisation in medicine is associated with a higher yield and quality, but might come with the downside of neglecting topics outside of the speciality. The theme of perceived nvHAP risk is related to tension for change in which dissatisfaction with the current situation serves as a driver for innovation.[26] Physical proximity of teams is an important finding to consider on an organisational level, especially for large institutions that tend to spread out teams to optimise bed occupancy rates.

Sustainability of interventions remains an under-assessed topic due to often limited funding periods. We found differences regarding sustainability between professional groups; although physiotherapists had well established processes in place, nurse and physician members of implementation teams struggled to induce lasting structural change. Cafazzo and colleagues suggested that a change of enduring structures is most effective for sustained implementation.[27] Finally, we found that implementation success correlated with intervention effectiveness quantitatively, corroborating the qualitative findings and guiding interpretation of varied intervention effectiveness between departments.

Our study has limitations. First, it was a single-centre study and the results might not be directly applicable to other settings. Nevertheless, by including nine departments with surgical and medical specialities, a broad patient and care-provider population was included. Second, the intervention period was planned to be 12 months, but the COVID-19 pandemic forced early termination, which affected the statistical solidity. Third, the implementation start date was at the discretion of each department as a pragmatic solution respecting their preparedness and capacity. We do not believe that the differences in start date challenge the findings, as the sensitivity analyses excluded a temporal trend and a regression to the mean of nvHAP incidence. Fourth, nvHAP surveillance and analysis of qualitative results were conducted by members of the project team. To limit desirability bias, we used rigorous qualitative research

methods[28] to maintain empathic neutrality during data collection and analysis. Some components of the nvHAP definition used for surveillance (eg, radiological criteria) leave room for subjective interpretation. Limiting the outcome measure to microbiologically confirmed nvHAP might have partially overcome this, but would have required a prohibitively larger sample size. Fifth, process measures were inherently difficult to assess. We chose to counterbalance this challenge by applying two evaluation methods but, due to the limitations of both methods, improved adherence might have been missed, especially in oral care and mobilisation. Sixth, length of hospital stay, an outcome measure mentioned in the study protocol, could not be assessed because of unavailability of the required data. Seventh, the bundle design precluded the possibility of examining the effect of single bundle elements. Moreover, the choice of bundle elements had to be pragmatic. It is known that oral care is associated with reduced nvHAP rates,[29] and intervention studies showed dysphagia screening effectiveness against nvHAP in patients with stroke.[30] Studies assessing the association between proton-pump inhibitors and pneumonia have shown ambiguous results,[31,32] thus leaving the value of this prevention measure when applied in isolation unresolved. Last, due to the rarity of nvHAP, our study was underpowered to detect an effect of the bundle on all-cause mortality in the main model. We found a statistically significant reduction in only one sensitivity analysis that included the CMI as an explanatory factor.

In conclusion, intervention effectiveness correlated with successful implementation of the nvHAP bundle. Individual and organisational determinants of this success could be described qualitatively. This description of implementation and intervention effectiveness could be especially helpful in the future upscaling of nvHAP prevention initiatives, but further research is warranted into the respective contributions of individual bundle elements and implementation in additional settings.

Contributors

AW, LC, MFH, M-TM, and HS contributed to the study concept and design. AW, KK, and RK calculated the sample sizes. AW, LC, MFH, and DS collected data. SvF and LH planned the statistical analysis. SvF conducted the statistical analysis. AW, LC, SvF, MFH, LH, and HS analysed the data and interpreted the results. AW, LC, and HS drafted the manuscript, and SvF, KK, MFH, DS, M-TM, RK, and LH provided critical review of the manuscript for important intellectual content. AW, MFH, and LC accessed and verified the data. All authors were responsible for the decision to submit for publication. All authors have seen and approved the final version of the Article.

Declaration of interests

We declare no competing interests.

Data sharing

To access the **data used in this Article** see https://doi.org/10.5281/zenodo.7212302

For the **R code used in these analyses** see https://doi.org/10.5281/zenodo.7084887

Data will be made available on Zenodo, together with a description of the variables. Access is restricted to researchers who apply with a methodologically sound proposal. The R code to reproduce analyses presented in the Article and its appendix is also shared on Zenodo.

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